REMARKS/ARGUMENTS

Claim 15 has been amended to recite additional properties of the claimed 38 kD protein as it occurs in its native state. Support for reciting that the 38 kD protein molecular weight is measured by SDS page, and appears as a broad band on SDS gels is provided at e.g., p. 11, lines 16-18 and 35-37. Support for the reciting that autoantibodies bind to subgroup of prediabetic and newly diagnosed individuals is provided at e.g., p. 14, lines 19-21, and 31-34.

Claim 15 stands rejected as anticipated or in the alternative obvious over Ko or Pak. This rejection is respectfully traversed.

The Examiner's allegation that the claim 15 did not contain any elements that distinguish the cited references is incorrect. Claim 15 required that the claimed protein has a pI in the range of 5/4 to 6.1 and an amphiphilic charge. As the Examiner acknowledges, Ko and Pak are silent as to these characteristics.

"Anticipation is established only when a single prior art reference discloses, expressly or under principles of inherency, each and every element of a claimed invention," RCA Corp v. Applied Digital Data Sys. Inc. 2212 USPQ 385, 388 (Fed. Cir. 1984). "Inherency ... *may not be established by probabilities or possibilities.*" *Mehl/Biophile v. Milgraum,* 52 USPQ2d 1303, 1305 (Fed. Cir. 1999) (emphasis supplied). If the evidence is in "equipoise," an inventor is "entitled to a patent." *In re Oetiker,* 24 USPQ2d 1443, 1447 (Fed. Cir. 1992) (Plager, J., concurring).

Here, it is undisputed that the proteins discussed in the cited references are not expressly disclosed to have a pI in the range of 5/4 to 6.1 and an amphiphilic charge. Moreover, the available evidence strongly indicates that the proteins of Ko and Pak do not inherently have such properties. The Baekkeskov declaration compares the proteins of Ko and Pak to Glima-38 and concludes that Glima-38 is a different protein from either the protein of Ko or that of Pak. The pI and amphiphilic charge of a protein are a consequence of its primary amino acid sequence. Different proteins have different amino acid sequences, and thus different pI's and other charge characteristics. Because Ko and Pak's proteins are different proteins than Glima 38,

there is no reason to think they have any amino acid sequence similarity or consequently have the same pI or other charge characteristics as Glima-38.

Dr. Baekkeskov is an expert in the field, and there is no basis for questioning her conclusion that Glima 38 is a different protein than Ko's and Pak's proteins. Indeed, the Examiner has not attempted to do so. Rather, the Examiner is effectively proposing that despite Ko and Pak's proteins being different to Glima 38, Ko and Pak's proteins might coincidentally have the same pI and amphiphilic charge as Glima 38, and thus be included within the scope of claim 15. Such a view is highly speculative. One it is established that Ko and Pak's proteins are different from Glima-38, there is no reason to expect any similarity of amino acid sequence or consequently of pI values or amphiphilic properties. Inherency cannot be established by probabilities or possibilities particularly one so remote as of different proteins coincidentally having the same pI and sharing amphiphilic properties.

Because Ko and Pak do not expressly or inherently disclose a protein having inter alia a pI in the range of 5/4 to 6.1 and an amphiphilic charge, the anticipation rejection should be withdrawn.

Once it is accepted that Ko and Pak do not disclose a protein having inter alia a pI in the range of 5/4 to 6.1 and an amphiphilic charge, no basis is apparent as to how the references could have rendered such a protein obvious. The Examiner has not identified any secondary references or general knowledge in the art as to how the teaching of Ko or Pak could be modified, and none is apparent. Accordingly, it is submitted that the obviousness rejection should be withdrawn as well.

Although it is maintained that claim 15 are distinguished for the reasons given above, the claim has been further amended to provide additional distinctions including particularly the recitation that the claimed protein runs as a broad band indicative of heterogeneity in size and/or charge. As previously noted the proteins of Ko and Pak run as a sharp band.

Claim 15 also stand rejected as allegedly anticipated by DeAizupurua. This rejection raises essentially the same issue described above. Dr. Baekkeskov has provided evidence that DeAisupurua's protein is different from Glima-38. The Examiner has not

questioned this conclusion. It follows that except for extremely unlikely coincidence, DeAizupurua's protein does not share the pI and amphiphilic character of Glima-38. Inherency cannot be established from such a remote possibility. Thus, the Examiner has not established that DeAizupurua discloses either expressly or inherently a protein having inter alia a pI in the range of 5/4 to 6.1 and an amphiphilic charge, as claimed.

Although it is maintained that claim 15 are distinguished for the reasons given above, the claim has been further amended to provide additional distinctions including particularly the recitation that the claimed protein runs as a broad band indicative of heterogeneity in size and/or charge. As previously noted the protein DeAizupurua runs as a sharp band.

Finally, it is noted that rejections over the references cited by the Examiner were extensively discussed and distinguished in the prosecution of two predecessor cases, both of which has issued. The present claims are allowable for at least the same reasons.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 650-326-2400.

Respectfully submitted,

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